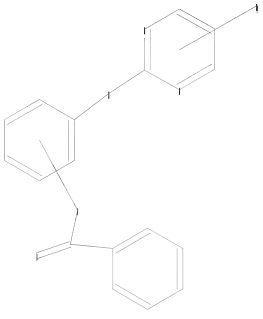
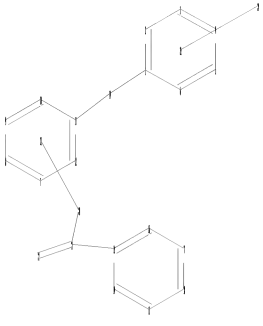
=>
Uploading C:\Program Files\Stnexp\Queries\10502291.str



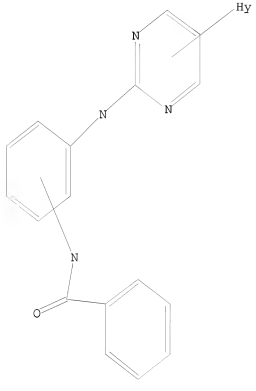


chain nodes :
19 20 21 22 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-19 11-19 15-21 20-21 21-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
exact/norm bonds :
1-19 11-19 20-21 21-22
exact bonds :
15-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom
Generic attributes :
24:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

```
Element Count :
Node 24: Limited
    C,C5
    N,N1
    O,O0
    S,S0
```

```
L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
```



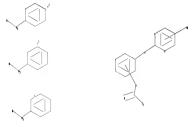

```
Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 11:54:00 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     2723 TO ITERATE

 73.4% PROCESSED     2000 ITERATIONS                                 9 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
```

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 51330 TO 57590
PROJECTED ANSWERS: 35 TO 455

L2 9 SEA SSS SAM L1

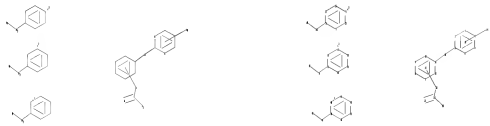
=> =>
Uploading C:\Program Files\Stnexp\Queries\10502291 (a).str



chain nodes :
19 20 21 22 24 28 29 36 37 44 45 50
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 30 31 32 33 34
35 38 39 40 41 42 43
chain bonds :
1-19 11-19 14-28 20-21 21-22 21-50 28-29 31-36 36-37 39-44 44-45
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18 30-31 30-35 31-32 32-33 33-34 34-35 38-39 38-43
39-40 40-41 41-42 42-43
exact/norm bonds :
1-19 11-19 20-21 21-22 21-50 28-29 36-37 44-45
exact bonds :
14-28 31-36 39-44
normalized bonds :

```
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18  30-31  30-35  31-32  32-33  33-34  34-35  38-39  38-43
39-40  40-41  41-42  42-43
isolated ring systems :
containing 1 : 7 : 13 : 30 : 38 :


G1:[*1],[*2],[*3]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:Atom  24:Atom  25:Atom  28:CLASS  29:Atom  30:Atom
 31:Atom  32:Atom  33:Atom  34:Atom  35:Atom  36:CLASS  37:Atom  38:Atom  39:Atom
40:Atom  41:Atom  42:Atom  43:Atom  44:CLASS  45:Atom  50:CLASS
Generic attributes :
24:
Saturation              : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System     : Monocyclic

Element Count :
Node 24: Limited
    C,C5
    N,N1
    O,O0
    S,S0




L3      STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l3 sss sam
SAMPLE SEARCH INITIATED 12:00:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      265 TO ITERATE

100.0% PROCESSED      265 ITERATIONS                                  8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:          4324 TO      6276
PROJECTED ANSWERS:                8 TO       329
```

```
L4             8 SEA SSS SAM L3

=> => s l3 sss ful
FULL SEARCH INITIATED 12:01:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      5275 TO ITERATE

100.0% PROCESSED     5275 ITERATIONS                                198 ANSWERS
SEARCH TIME: 00.00.01

L5           198 SEA SSS FUL L3

=> => s l5
L6          3032 L5

=> => ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 1719

L7     SCREEN CREATED

=>
Uploading C:\Program Files\Stnexp\Queries\10502291 (b).str
```



```
chain nodes :
19  20  21  22  24  28  29  36  37  44  45  50
```

```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  30  31  32  33  34
35  38  39  40  41  42  43
chain bonds :
1-19  11-19  14-28  20-21  21-22  21-50  28-29  31-36  36-37  39-44  44-45
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18  30-31  30-35  31-32  32-33  33-34  34-35  38-39  38-43
39-40  40-41  41-42  42-43
exact/norm bonds :
1-19  11-19  20-21  21-22  21-50  28-29  36-37  44-45
exact bonds :
14-28  31-36  39-44
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18  30-31  30-35  31-32  32-33  33-34  34-35  38-39  38-43
39-40  40-41  41-42  42-43
isolated ring systems :
containing 1 : 7 : 13 : 30 : 38 :


G1:[*1],[*2],[*3]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:Atom  24:Atom  25:Atom  28:CLASS  29:Atom  30:Atom
 31:Atom  32:Atom  33:Atom  34:Atom  35:Atom  36:CLASS  37:Atom  38:Atom  39:Atom
40:Atom  41:Atom  42:Atom  43:Atom  44:CLASS  45:Atom  50:CLASS
Generic attributes :
24:
Saturation              : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System    : Monocyclic

Element Count :
Node 24: Limited
    C,C5
    N,N1
    O,O0
    S,S0
```

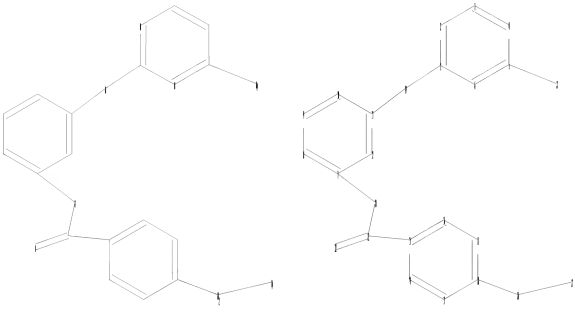
L8 STRUCTURE UPLOADED

=> que L8 AND L7

L9 QUE L8 AND L7

=> d 19
L9 HAS NO ANSWERS
L7 SCR 1719

```
L8              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L9              QUE  L8 AND L7


=> s l9 sss sam
SAMPLE SEARCH INITIATED 12:07:26 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L10           0 SEA SSS SAM L8 AND L7

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2005 AND 1842

L11   SCREEN CREATED

=> screen 2016 OR  2026 OR  2039 OR  2045 OR  2047

L12   SCREEN CREATED

=>
Uploading C:\Program Files\Stnexp\Queries\10502291 (c).str
```

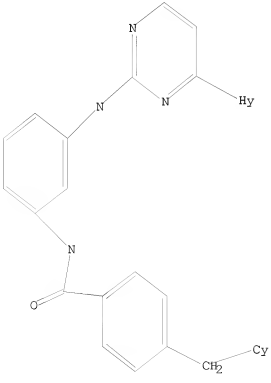


chain nodes :
19 20 21 22 23 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-19 5-23 7-20 11-19 15-21 18-26 20-21 21-22 26-27
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
exact/norm bonds :
1-19 5-23 7-20 11-19 20-21 21-22 26-27
exact bonds :
15-21 18-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18
14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 7 : 13 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 26:CLASS 27:CLASS
Generic attributes :
23:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic
27:
Type of Ring System : Monocyclic

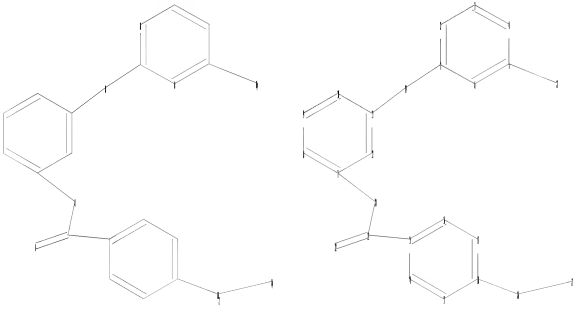
```
Element Count :
Node 23: Limited
    C,C5
    N,N1
    O,O0
    S,S0
```

```
L13     STRUCTURE UPLOADED

=> que L13 AND L11 NOT L12

L14  QUE L13 AND L11 NOT L12

=> d l14
L14 HAS NO ANSWERS
L11             SCR 2005 AND 1842
L12             SCR 2016 OR 2026 OR 2039 OR 2045 OR 2047
L13             STR
```



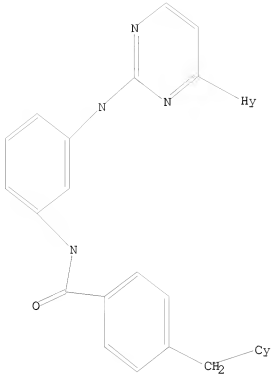

```
Structure attributes must be viewed using STN Express query preparation.
L14             QUE  L13 AND L11 NOT L12
```

```
=> s l14 sss sam
SAMPLE SEARCH INITIATED 12:12:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       19 TO ITERATE

100.0% PROCESSED       19 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:           119 TO      641
PROJECTED ANSWERS:                5 TO      234

L15           5 SEA SSS SAM L13 AND L11 NOT L12

=> => ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2005 AND 1842

L16   SCREEN CREATED

=> screen 2016 OR  2026 OR  2039 OR  2045 OR  2047 OR  2127

L17   SCREEN CREATED

=>
Uploading C:\Program Files\Stnexp\Queries\10502291 (d).str
```



```
chain nodes :
19  20  21  22  23  26  27
ring nodes :
```

```
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
1-19  5-23  7-20  11-19  15-21  18-26  20-21  21-22  26-27
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18
exact/norm bonds :
1-19  5-23  7-20  11-19  20-21  21-22  26-27
exact bonds :
15-21  18-26
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  13-14  13-18
14-15  15-16  16-17  17-18
isolated ring systems :
containing 1 : 7 : 13 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:Atom  26:CLASS  27:CLASS
Generic attributes :
23:
Saturation              : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System    : Monocyclic
27:
Type of Ring System    : Monocyclic

Element Count :
Node 23: Limited
    C,C5
    N,N1
    O,O0
    S,S0




L18     STRUCTURE UPLOADED

=> que L18 AND L16 NOT L17

L19  QUE L18 AND L16 NOT L17

=> d l19
L19 HAS NO ANSWERS
L16                 SCR 2005 AND 1842
L17                 SCR 2016 OR 2026 OR 2039 OR 2045 OR 2047 OR 2127
L18                 STR
```



Structure attributes must be viewed using STN Express query preparation.
L19 QUE L18 AND L16 NOT L17

=> s l19 sss sam
SAMPLE SEARCH INITIATED 12:15:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22 TO 418
PROJECTED ANSWERS: 1 TO 80

L20 1 SEA SSS SAM L18 AND L16 NOT L17

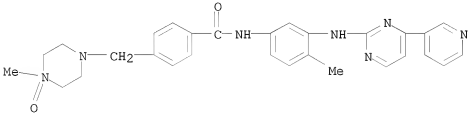
=> => s l19 sss ful
FULL SEARCH INITIATED 12:15:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 127 TO ITERATE

100.0% PROCESSED 127 ITERATIONS 26 ANSWERS
SEARCH TIME: 00.00.01

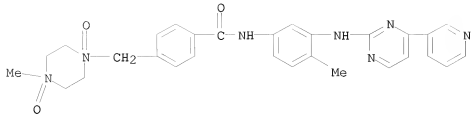
L21 26 SEA SSS FUL L18 AND L16 NOT L17

```
=> => s l21
L22           14 L21

=> d l22 1-14 bib,ab,hitstr
```

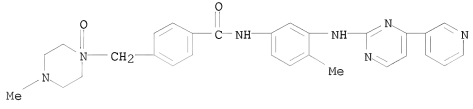
L22 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:345353 CAPLUS
DN 147:39589
TI Identification of imatinib mesylate degradation products obtained under stress conditions
AU Szczepek, W. J.; Kosmacinska, B.; Bielejewska, A.; Luniewski, W.; Skarzynski, M.; Rozmarynowska, D.
CS Pharmaceutical Research Institute, Warsaw, 01-793, Pol.
SO Journal of Pharmaceutical and Biomedical Analysis (2007), 43(5), 1682-1691
CODEN: JPBADA; ISSN: 0731-7085
PB Elsevier B.V.
DT Journal
LA English
AB In this paper, the decomposition of imatinib mesylate (ImM) under hydrolytic (neutral, acidic, alkaline), oxidative and photolytic conditions was studied. The imatinib mesylate is practically photostable and stable under neutral conditions. The main degradation products under acidic and alkaline conditions are compds.: 4-methyl-N 3-(4-pyridin-3-yl-pyrimidyn-2-yl)-benzene-1,3-diamine and 4-(4-methyl-piperazin-1-ylmethyl)-benzoic acid. The main degradation products under oxidation conditions, i.e. 4-[(4-methyl-4-oxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide, 4-[(4-methyl-1-oxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide and 4-[(4-methyl-1,4-dioxido-piperazin-1-yl)-methyl]-N-[4-methyl-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-phenyl]-benzamide, were isolated from the reaction mixts. and identified by the HPLC, 1H NMR and MS techniques. During stress study the suitability of the proposed HPLC method to control purity of the samples was verified.
IT 571186-91-9 571186-93-1 938082-57-6
RL: OCU (Occurrence, unclassified); PEP (Physical, engineering or chemical process); OCCU (Occurrence); PROC (Process)
(imatinib mesylate degradation products identification obtained under stress conditions)
RN 571186-91-9 CAPLUS
CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 571186-93-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1,4-dioxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 938082-57-6 CAPLUS
CN Benzamide, 4-[(4-methyl-1-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

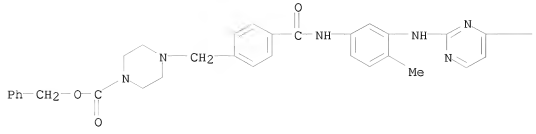


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:187945 CAPLUS
DN 146:437129
TI Synthesis and positron emission tomography studies of carbon-11-labeled imatinib (Gleevec)
AU Kil, Kun-Eek; Ding, Yu-Shin; Lin, Kuo-Shyan; Alexoff, David; Kim, Sung Won; Shea, Colleen; Xu, Youwen; Muench, Lisa; Fowler, Joanna S.
CS Medical Department, Brookhaven National Laboratory, Upton, NY, 11973, USA
SO Nuclear Medicine and Biology (2007), 34(2), 153-163
CODEN: NMBIEO; ISSN: 0969-8051
PB Elsevier Inc.
DT Journal
LA English
AB Introduction: Imatinib mesylate (Gleevec) is a well known drug for treating chronic myeloid leukemia and gastrointestinal stromal tumors. Its active ingredient, imatinib (4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridyl)-2-pyrimidinyl]amino]phenyl]benzamide), blocks the activity of several tyrosine kinases. Here we labeled imatinib with carbon-11 as a tool for determining the drug distribution and pharmacokinetics of imatinib, and we carried out positron emission tomog. (PET) studies in baboons. Methods: [N-11C-methyl]imatinib was synthesized from [11C]methyl iodide and norimatinib was synthesized by the demethylation of imatinib (isolated from Gleevec tablets) according to a patent procedure [Collins JM, Klecker RW Jr, Anderson LW, Imaging of drug accumulation as a guide to antitumor therapy. US Patene 20030198594A1, 2003.]. Norimatinib was also synthesized from the corresponding amine and acid. PET studies were carried out in three baboons to measure pharmacokinetics in the brain and peripheral organs and to determine the effect of a therapeutic dose of imatinib. Log D and plasma protein binding were also measured. Results: [N-11C-methyl]imatinib uptake in the brain is negligible (consistent with P-glycoprotein-mediated efflux); it peaks and clears rapidly from the heart, lungs and spleen. Peak uptake and clearance occur more slowly in the liver and kidneys, followed by accumulation in the gallbladder and urinary bladder. Pretreatment with imatinib did not change uptake in the heart, lungs, kidneys and spleen, and increased uptake in the liver and gallbladder. Conclusions: [N-11C-methyl]imatinib has potential for assessing the regional distribution and kinetics of imatinib in the human body to determine whether the drug targets tumors and to identify other organs to which the drug or its labeled metabolites distribute. Paired with tracers such as 2'deoxy-2'-[18F]fluoro-D-glucose (18FDG) and 3'deoxy-3'-[18F]fluorothymidine (18FLT), [N-11C-methyl]imatinib may be a useful radiotracer for planning chemotherapy, for monitoring response to treatment and for assessing the role of drug pharmacokinetics in drug resistance.
IT 934683-38-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and PET studies of 11C-labeled imatinib for determining imatinib pharmacokinetics)
RN 934683-38-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]-, phenylmethyl ester (CA INDEX NAME)

not prior

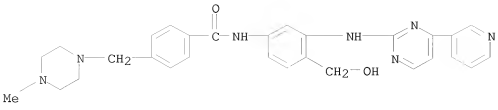
PAGE 1-A



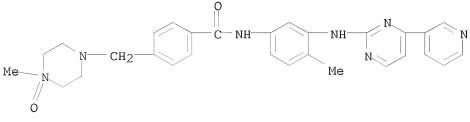
PAGE 1-B

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1068885 CAPLUS
DN 143:338914
TI Metabolism and disposition of imatinib mesylate in healthy volunteers
AU Gschwind, Hans-Peter; Pfaar, Ulrike; Waldmeier, Felix; Zollinger, Markus; Sayer, Claudia; Zbinden, Peter; Hayes, Michael; Pokorny, Rolf; Seiberling, Michael; Ben-Am, Monique; Peng, Bin; Gross, Gerhard
CS Exploratory Development/Drug Metabolism & Pharmacokinetics, Novartis Pharma AG, Basel, Switz.
SO Drug Metabolism and Disposition (2005), 33(10), 1503-1512 not prior
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Imatinib mesylate (GLEEVEC, GLIVEC, formerly STI571) has demonstrated unprecedented efficacy as first-line therapy for treatment for all phases of chronic myelogenous leukemia and metastatic and unresectable malignant gastrointestinal stromal tumors. Disposition and biotransformation of imatinib were studied in four male healthy volunteers after a single oral dose of 239 mg of 14C-labeled imatinib mesylate. Biol. fluids were analyzed for total radioactivity, imatinib, and its main metabolite CGP74588. Metabolite patterns were determined by radio-high-performance liquid chromatog. with off-line microplate solid scintillation counting and characterized by liquid chromatog.-mass spectrometry. Imatinib treatment was well tolerated without serious adverse events. Absorption was rapid (tmax 1-2 h) and complete with imatinib as the major radioactive compound in plasma. Maximum plasma concns. were 0.921±0.095 μg/mL (mean ± S.D., n = 4) for imatinib and 0.115±0.026 μg/mL for the pharmacol. active N-desmethyl metabolite (CGP74588). Mean plasma terminal elimination half-lives were 13.5±0.9 h for imatinib, 20.6±1.7 h for CGP74588, and 57.3±12.5 h for 14C radioactivity. Imatinib was predominantly cleared through oxidative metabolism Approx. 65 and 9% of total systemic exposure [AUC0-24 h (area under the concentration time curve) of radioactivity] corresponded to imatinib and CGP74588, resp. The remaining proportion corresponded mainly to oxidized derivs. of imatinib and CGP74588. Imatinib and its metabolites were excreted predominantly via the biliary-fecal route. Excretion of radioactivity was slow with a mean radiocarbon recovery of 80% within 7 days (67% in feces, 13% in urine). Approx. 28 and 13% of the dose in the excreta corresponded to imatinib and CGP74588, resp.
IT 571186-90-8, AFN 911 571186-91-9, CGP 71422
571186-92-0, CGP 72383 571186-94-2, APG 049
571186-95-3, APG 050 571186-95-3D, glucuronides
865487-49-6 865487-49-6D, glucuronides
865487-52-1 865487-52-1D, glucuronides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolism and disposition of imatinib mesylate in healthy volunteers)
RN 571186-90-8 CAPLUS
CN Benzamide, N-[4-(hydroxymethyl)-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



RN 571186-91-9 CAPLUS
CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 571186-92-0 CAPLUS
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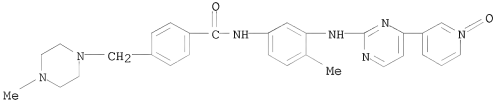
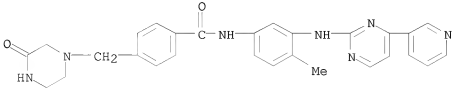
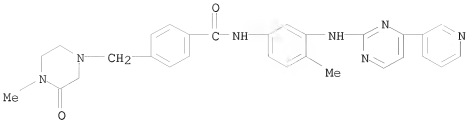


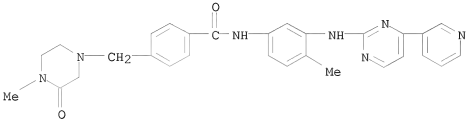
RN 571186-94-2 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(3-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



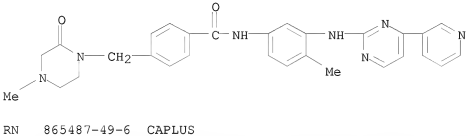
RN 571186-95-3 CAPLUS
CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



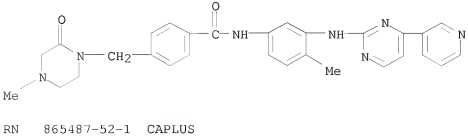
RN 571186-95-3 CAPLUS
CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 865487-49-6 CAPLUS
CN Benzamide, 4-[(4-methyl-2-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

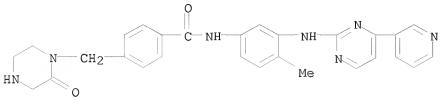


RN 865487-49-6 CAPLUS
CN Benzamide, 4-[(4-methyl-2-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

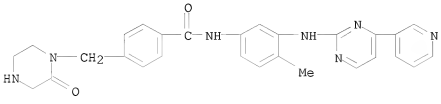


RN 865487-52-1 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(2-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



RN 865487-52-1 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(2-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:614536 CAPLUS
DN 143:115392
TI Preparation of conjugated small molecules for diagnostic and therapeutic use
IN Grotzfeld, Robert M.; Milanov, Zdravko V.; Patel, Hitesh K.; Lai, Andiliy G.; Mehta, Shamal A.; Lockhart, David J.
PA Ambit Biosciences Corp., USA
SO U.S. Pat. Appl. Publ., 63 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

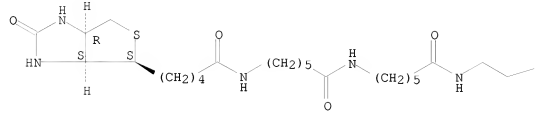
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005153371	A1	20050714	US 2005-31638	20050107
	AU 2005204428	A1	20050728	AU 2005-204428	20050107
	CA 2551495	A1	20050728	CA 2005-2551495	20050107
	WO 2005067644	A2	20050728	WO 2005-US456	20050107
	WO 2005067644	A3	20051013		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1711825	A2	20061018	EP 2005-705221	20050107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	JP 2007521338	T	20070802	JP 2006-549423	20050107
PRAI	US 2004-535173P	P	20040107		
	US 2004-557941P	P	20040330		
	WO 2005-US456	W	20050107		

not prior

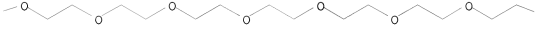
AB Provided herein are linker compds. and conjugates that include the linker compds. In one embodiment, the linker compds. comprise 2 or 3 residues of 6-aminohexanoic acid and optionally 7-10 residues of polyethyleneglycol (PEG). The linker compds. are useful in forming conjugates with one or more components useful in biopharmaceutical or bioanal. applications. In particular, the biopharmaceutically useful compds. are kinase inhibitors. The conjugates described herein have utility in a variety of diagnostic, separation, and therapeutic applications. Thus, I was prepared from SB 202190, PEG-azide and the biotin-linker compound
IT 857892-08-1P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of conjugated biotins for diagnostic and therapeutic use)
RN 857892-08-1 CAPLUS
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, hexahydro-N-[37-[4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]-1-piperazinyl]-6,13-dioxo-17,20,23,26,29,32,35-heptaoxa-7,14-diazaheptatriacont-1-yl]-2-oxo-, (3aS,4S,6aR)- (CA INDEX NAME)

Absolute stereochemistry.

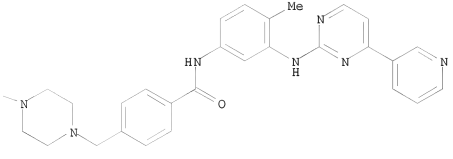
PAGE 1-A



PAGE 1-B



PAGE 1-C



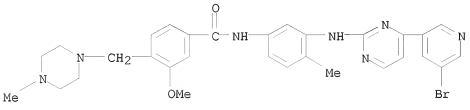
L22 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:612254 CAPLUS
DN 143:133396
TI Preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase inhibitors
IN Asaki, Tetsuo; Sugiyama, Yukiteru; Segawa, Jun
PA Nippon Shinyaku Co., Ltd., Japan
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005063709	A1	20050714	WO 2004-JP19553	20041227
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004309248	A1	20050714	AU 2004-309248	20041227
	CA 2551529	A1	20050714	CA 2004-2551529	20041227
	EP 1702917	A1	20060920	EP 2004-807908	20041227
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	CN 1898208	A	20070117	CN 2004-80039048	20041227
	BR 2004018074	A	20070417	BR 2004-18074	20041227
	MX 2006PA07237	A	20060818	MX 2006-PA7237	20060622
	IN 2006CN02337	A	20070706	IN 2006-CN2337	20060626
PRAI	JP 2003-431398	A	20031225		
	WO 2004-JP19553	W	20041227		

not prior

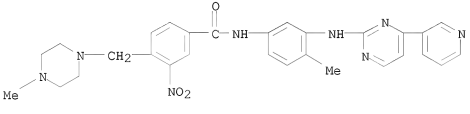
OS MARPAT 143:133396
AB The title compds. I (R1 represents CH2R11 (R11 represents a nitrogenous saturated heterocyclic group), etc.; R2 represents alkyl, halogeno, haloalkyl, etc.; R3 represents hydrogen, halogeno, alkoxy; Het1 represents Q1, etc.; and Het2 represents pyrimidinyl, etc.) are prepared Thus 3-difluoromethyl-4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl]benzamide was prepared from 4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]aniline and 3-difluoromethyl-4-(4-methylpiperazin-1-ylmethyl)benzoyl chloride HCl salt. In an assay (for cell proliferation inhibiting activity) using K562 cells, compds. of this invention showed IC50 values of < 0.00001 μM to 0.001 μM. Formulations are given.
IT 859211-72-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase inhibitors)
RN 859211-72-6 CAPLUS

CN Benzamide, N-[3-[[4-(5-bromo-3-pyridinyl)-2-pyrimidinyl]amino]-4-methylphenyl]-3-methoxy-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



IT 641615-04-5P 641615-05-6P 641615-07-8P
641615-08-9P 641615-15-8P 641615-21-6P
859213-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclyl moiety-containing amides as BCR-ABL tyrosine kinase
inhibitors)

RN 641615-04-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-3-nitro- (CA INDEX NAME)



RN 641615-05-6 CAPLUS
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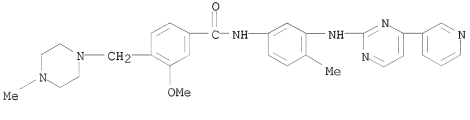

RN 641615-07-8 CAPLUS
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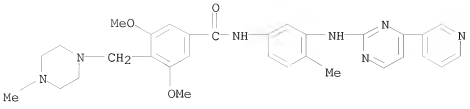
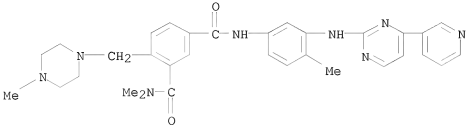


RN 641615-08-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N3,N3-dimethyl-4-[(4-methyl-1-piperazinyl)methyl]-N1-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 641615-15-8 CAPLUS
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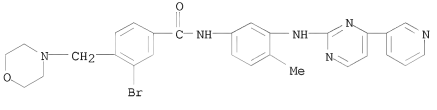
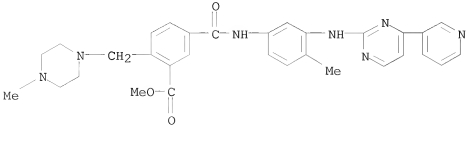
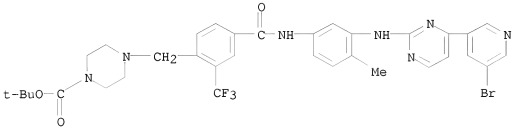


RN 641615-21-6 CAPLUS
CN Benzoic acid, 2-[(4-methyl-1-piperazinyl)methyl]-5-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)



RN 859213-57-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[3-[[4-(5-bromo-3-pyridinyl)-2-pyrimidinyl]amino]-4-methylphenyl]amino]carbonyl]-2-(trifluoromethyl)phenyl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1080884 CAPLUS
DN 142:56339
TI Process for the preparation of the anti-cancer drug imatinib and its analogs via aminolysis of a (chloromethyl)benzamide intermediate
IN Kompella, Amala; Bhujanga Rao, Adibhatla Kali Sathya; Venkaiah Chowdary, Nannapaneni; Srinivas, Rachakonda
PA Natco Pharma Limited, India
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2

not prior

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004108699	A1	20041216	WO 2003-IN211	20030606
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003242988	A1	20050104	AU 2003-242988	20030606
PRAI	WO 2003-IN211	A	20030606		

OS CASREACT 142:56339

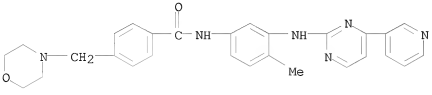
AB The invention discloses a process for the manufacture of imatinib [I; X = 4-methylpiperazin-1-yl] and three of its new analogs I [X = morpholin-4-yl, piperidin-1-yl, and imidazol-1-yl] through aminolyis of the intermediate I [X = Cl]. The mesylate (methanesulfonate) salt of imatinib is a popular life-saving drug, used to treat chronic myelogenous leukemia (CML). The other compds. are claimed as protein tyrosine kinase inhibitors (no data). The new process involves fewer steps (7) than the 9 steps in the known process disclosed in EP 0564409 and US 55211584, making the new process simple and cost effective. Yields are fairly high in all steps (65-90%), as compared to 20-50% realized by the prior art process. Reaction times are fairly low (8-10 h) in all steps, as compared to the time (12-25 h) for most of the stages in the prior art process. Obnoxious, foul smelling, and difficult-to-handle reagents are avoided, making the process safe and environmentally safe for com. application. Column chromatog., which is not practical on com. scale, is avoided at all stages. Consequently the process is simple and economical. Thus, 2-amino-4-nitrotoluene in BuOH was treated with HNO3 and then with aqueous cyanamide, and the mixture was heated at 90-95° for 12 h, to give 61% yield of 2-methyl-5-nitrophenylguanidine nitrate (II) on a 22-kg scale, with simple recovery of pure, unreacted 2-amino-4-nitrotoluene from the mother liquors, also on a multi-kg scale. Cyclization of II with 3-(dimethylamino)-1-(3-pyridyl)-2-propen-1-one in refluxing BuOH in the presence of NaOH for 10 h gave intermediate III quant., with III being isolated in 88% yield on a 21-kg scale. This was followed by reduction of the nitro group of III, using SnCl2 in concentrated HCl, to give the corresponding amine in 61.5% yield, on a 10-kg scale. The amine was amidated with 4-(ClCH2)C6H4COCl (preparation given) using Et3N in CHCl3, giving the (chloromethyl)benzamide intermediate I [X = Cl] in 70% yield on a 13.9-kg

scale. This compound reacted with N-methylpiperazine in DMF over 4 h at 20-40°, giving imatinib free base after extraction into CHCl3, carbon treatment, evaporation, and trituration with EtOAc. Imatinib was obtained in 61% yield, 99.8% purity by HPLC, and on a 9.8-kg scale. The other three products I were obtained almost identically, using different amines in the final step.

IT 404843-98-7P, 4-(Morpholinomethyl)-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; manufacture of imatinib and analogs via aminolysis of (chloromethyl)benzamide intermediate)

RN 404843-98-7 CAPLUS

CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1060780 CAPLUS
DN 142:38275
TI Preparation of N-phenyl-2-pyrimidine-amine derivatives as anticancer agents and process for the preparation thereof
IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jin; Lee, Gong-Yeal; Kim, Hong-Youb; Woo, Seok-Hun; Kim, Yong-Seok; Bae, Woo-Chul; Lee, Sun-Ahe; Han, Byoung-Cheol
PA Il Yang Pharm. Co., Ltd., S. Korea
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 446,446, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004248918	A1	20041209	US 2004-806834	20040322
PRAI KR 2003-28669	A	20030506		
US 2003-446446	B2	20030528		

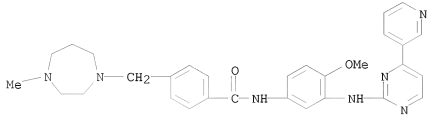
not prior

OS MARPAT 142:38275
AB The title compds. (I) [R1 = 3- or 4-pyridyl; R2, R3 = H, lower alkyl; R6, R7 = Q; wherein X = O, NH; n= 0, 1; R9 = C5-10 9 aliphatic radical, 5- to 7-membered (un)saturated monocyclic radical, or bi- or tricyclic radical optionally combined with benzene ring, each of which has 1 to 3 hetero atoms selected from a group consisting of N, O, and S, piperazinyl or homopiperazinyl each of which is substituted by lower alkyl; R4, R5, R7, R8 = H or one or two thereof each represent halogen, lower alkyl, or lower alkoxy; when R6 is Q, or one or two of R4, R5, R6, and R8 each represent halogen, lower alkyl, or lower alkoxy; when R7 is Q, provided that R6 or R7 represents Q wherein n = 0 and R9 = 4-methylpiperazine, then one or more of R4, R5, R7, and R8, or one or more of R4, R5, R6, and R8 are halogen] or salts thereof are prepared These compds. show a superior effect on lung cancer, gastric cancer, colon cancer, pancreatic cancer, hepatoma, prostatic cancer, breast cancer, chronic or acute leukemia, hematol. malignancy, encephalophyma, bladder cancer, rectal cancer, or cervical cancer of warm-blooded animals. The present invention also relates to a process for preparing the compound I, and to a pharmaceutical composition for the
treatment of the above various diseases, which comprises an effective amount of the compound as an active ingredient together with pharmaceutically acceptable inert carriers. Thus, 3-dimethylamino-1-(3-pyridyl)-2-propen-1-one was cyclocondensed with 2-methyl-5-nitrophenylguanidine nitrate in the presence of sodium hydroxide in isopropanol under reflux for 18 h to give N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine which was reduced by stannous chloride dihydrate in EtOAc/ethanol under reflux for 4 h to give N-(5-amino-2-methylphenyl)-4-(3-pyridyl)-2-pyrimidineamine (II). II underwent amidation with 4-chloromethylbenzoyl chloride in Et3N in THF under reflux for 4 h to give N-[5-(4-chloromethylbenzoylamino)-2-methylphenyl]-4-(3-pyridyl)-2-pyrimdineamine which was stirred with pyridine for 30 min and then refluxed with N-methylhomopiperazine for 12 h to give 4-(4-methylhomopiperazin-1-ylmethyl)-N-[4-methyl-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide (III). III methanesulfonate and 4-[(4-methylpiperazin-1-ylamino)methyl]-N-[4-methyl-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide methanesulfonate showed IC50 of 1.20 and <0.10 μg/mL, resp., against the growth of K562 cells.
IT 796738-40-4P, 4-(4-Methylhomopiperazin-1-ylmethyl)-N-[4-methoxy-3-

[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-phenylpyrimidine-2-amine derivs. as anticancer agents)

RN 796738-40-4 CAPLUS

CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



L22 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:996162 CAPLUS
DN 141:424205
TI New N-phenyl-2-pyrimidine-amine derivatives related to imatinib mesylate, useful as antitumor agents, and process for their preparation
IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jin; Lee, Gong-Yeal; Kim, Hong-Youb; Woo, Seok-Hun; Kim, Yong-Seok; Bae, Woo-chul; Lee, Sun-Ahe; Han, Byoung-Cheol
PA Il Yang Pharm. Co. Ltd., S. Korea
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
not prior
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004099187	A1	20041118	WO 2004-KR611	20040319
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	KR 2004095155	A	20041112	KR 2004-17594	20040316
PRAI	KR 2003-28669	A	20030506		

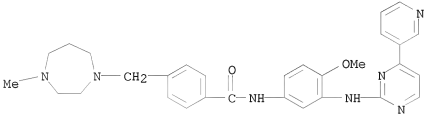
OS MARPAT 141:424205
AB The invention relates to N-phenyl-2-pyrimidine-amine derivs. and their salts, which show superior action against lung cancer, gastric cancer, colon cancer, pancreatic cancer, hepatoma, prostatic cancer, breast cancer, chronic or acute leukemia, hematol. malignancy, encephalophyma, bladder cancer, rectal cancer, or cervical cancer, etc., in warm-blooded animals. The invention also relates to a process for preparing the compds., and to pharmaceutical compns. for the treatment of cancer, etc., which comprise the compds. as active ingredients, together with pharmaceutically acceptable inert carriers. Specifically claimed are compds. I and salts [wherein: R1 = 3-pyridyl or 4-pyridyl; R2, R3 = (independently) H or lower alkyl; R6 or R7 = -NHCO-p-C6H4-CH2XnR9; X = O or NH; n = 0-1; R9 = C5-10 aliphatic, or 5- to 7-membered (un)saturated monocycle, or a bi- or tricyclic radical optionally combined with a benzene ring, each with 1-3 N/O/S heteroatoms, or (homo)piperazinyl substituted by lower alkyl; 1-2 of R4, R5, R6/R7, and R8 = halo, lower alkyl, or lower alkoxy; others = H; provided that when R6 or R7 = said radical and n = 0 and R9 = 4-methylpiperazinyl, then one or more of R4, R5, R6/R7, and R8 is halo]. For example, 3-acetylpyridine was converted in 3 steps to N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine. This nitro compound was reduced to the amine with SnCl2, and the amine was amidated with 4-(ClCH2)C6H4COCl. The obtained 4-(chloromethyl)benzamide derivative was coupled with 1-amino-4-methylpiperazine to give invention compound II, which was converted to the methanesulfonate salt (III). The latter was more than 5-fold more potent than imatinib mesylate against the human CML cell line K562, and was at least as active against other cell lines. Other compds. I showed different spectra of superiority to imatinib mesylate

against the various cancer cell lines. Compound IV (mesylate) had excellent, dose-related therapeutic activity against sarcoma-180 in ICR mice, giving an inhibition ratio of 63.0% at 50 mg/kg i.v. In an oral pharmacokinetic assay in rats, III roughly matched the performance of imatinib mesylate (Tmax, Cmax, and AUC) at half the dosage. III also showed no acute toxicity toward mice at a dose of 2000 mg/kg orally. IV mesylate had an i.v. LD50 of 75-100 mg/kg in mice, still much safer than cisplatin (11 mg/kg i.v.). Although several compds. I are preferred with respect to protein kinase inhibition (no data), II is particularly preferred. Therefore III and IV mesylate are expected to be new and potent therapeutic agents for the treatment of the aforementioned cancers, in addition to CML.

IT 796738-40-4P, 4-[(4-Methylhomopiperazin-1-yl)methyl]-N-[4-methoxy-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of phenylpyrimidinamine derivs. related to imatinib mesylate as antitumor agents)

RN 796738-40-4 CAPLUS

CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:996161 CAPLUS
DN 141:424204
TI New N-phenyl-2-pyrimidine-amine derivatives related to imatinib mesylate, useful as antitumor agents, and process for the preparation thereof
IN Kim, Dong-Yeon; Kim, Jae-Gun; Cho, Dae-Jn; Lee, Gong-Yeal; Kim, Hong-Youb; Woo, Seok-Hun; Bae, Woo-chul; Lee, Sun-Ahe; Han, Byoung-Ceol
PA Il Yang Pharm Co., Ltd., S. Korea
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099186	A1	20041118	WO 2003-KR1029	20030526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003232650	A1	20041126	AU 2003-232650	20030526
KR 2004095155	A	20041112	KR 2004-17594	20040316
PRAI KR 2003-28669	A	20030506		
WO 2003-KR1029	W	20030526		

not prior

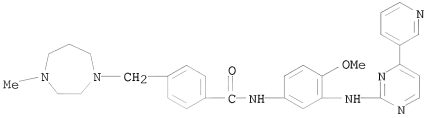
OS MARPAT 141:424204
AB The invention relates to N-phenyl-2-pyrimidine-amine derivs. and their salts, which show superior action against tumors, lung cancer, gastric cancer, etc., in warm-blooded animals. The invention also relates to a process for preparing the compds., and to pharmaceutical compns. for the prevention and treatment of cancer, etc., which comprise the compds. as active ingredients. Specifically claimed are compds. I and salts [wherein: R1 = 3-pyridyl or 4-pyridyl; R2, R3 = (independently) H or lower alkyl; R6 or R7 = -NHCO-p-C6H4-CH2XnR9; X = O or NH; n = 0-1; R9 = C5+ aliphatic or heterocycle, or (homo)piperazinyl substituted by lower alkyl; 1-2 of R4, R5, R6/R7, and R8 = halo, lower alkyl, or lower alkoxy; others = H; provided that when R6 or R7 = said radical and n = 0 and R9 = 4-methylpiperazinyl, then one or more of R4, R5, R6/R7, and R8 is halo]. For example, 3-acetylpyridine was converted in 3 steps to N-(2-methyl-5-nitrophenyl)-4-(3-pyridyl)-2-pyrimidineamine. This nitro compound was reduced to the amine with SnCl2, and the amine was amidated with 4-(ClCH2)C6H4COCl. The obtained 4-(chloromethyl)benzamide derivative was coupled with 1-amino-4-methylpiperazine to give invention compound II, which was converted to the methanesulfonate salt (III). The latter was more than 5-fold more potent than imatinib mesylate against the human CML cell line K562, and was at least as active against other cell lines. Other compds. I showed different spectra of superiority to imatinib mesylate against the various cancer cell lines. In an oral pharmacokinetic assay in rats, III roughly matched the performance of imatinib mesylate (Tmax, Cmax, and AUC) at half the dosage. III also showed no acute toxicity toward mice at a dose of 2000 mg/kg orally. Although several compds. I are preferred with respect to protein kinase inhibition (no data), II is

particularly preferred.

IT 796738-40-4P, 4-[(4-Methylhomopiperazin-1-yl)methyl]-N-[4-methoxy-3-[[4-(pyridin-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of phenylpyrimidinamine derivs. related to imatinib mesylate as antitumor agents)

RN 796738-40-4 CAPLUS

CN Benzamide, 4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]-N-[4-methoxy-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:589375 CAPLUS
DN 141:140459
TI Preparation of sulfamides as anti-cancer agents
IN Flynn, Daniel L.; Petrillo, Peter A.
PA Deciphera Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

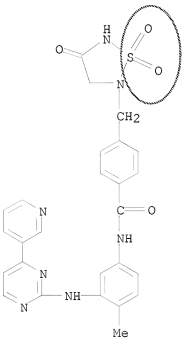
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060305	A2	20040722	WO 2003-US41425	20031226
	WO 2004060305	A3	20050210		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004171075	A1	20040902	US 2003-746545	20031224
	US 2004176395	A1	20040909	US 2003-746607	20031224
	US 7279576	B2	20071009		
	CA 2511840	A1	20040722	CA 2003-2511840	20031226
	AU 2003303639	A1	20040729	AU 2003-303639	20031226
	EP 1590344	A2	20051102	EP 2003-814980	20031226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003017863	A	20051206	BR 2003-17863	20031226
	CN 1756849	A	20060405	CN 2003-80110049	20031226
	CN 1791596	A	20060621	CN 2003-80110048	20031226
	JP 2006519765	T	20060831	JP 2005-508623	20031226
	IN 2005CN01433	A	20070302	IN 2005-CN1433	20050628
PRAI	US 2002-437304P	P	20021231		
	US 2002-437403P	P	20021231		
	US 2002-437415P	P	20021231		
	US 2002-437487P	P	20021231		
	US 2003-463804P	P	20030418		
	US 2003-746545	A	20031224		
	US 2003-746607	A	20031224		
	WO 2003-US41425	W	20031226		

OS MARPAT 141:140459
AB Sulfamides, such as I, were prepared for use as anticancer agents which act by modulating the activation states of abl or bcr-abl α-kinase proteins. Thus, 4-HO2CC6H4CH2NHSO2NHCOR [R = pyrrolidino], prepared from 4-MeO2CC6H4CH2NH2 and pyrrolidine, was treated with the pyrimidinylaminoaniline fragment to give I, which showed 10% inhibition of non-phosphorylated abl kinase at 10μM.
IT 726192-44-5P 726192-54-7P 726192-56-9P
726192-57-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of sulfamides as anti-cancer agents)

RN 726192-44-5 CAPLUS

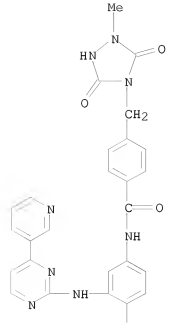
CN Benzamide, 4-[(1,1-dioxido-4-oxo-1,2,5-thiadiazolidin-2-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 726192-54-7 CAPLUS

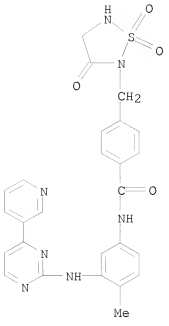
CN Benzamide, 4-[(1-methyl-3,5-dioxo-1,2,4-triazolidin-4-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

PAGE 1-A



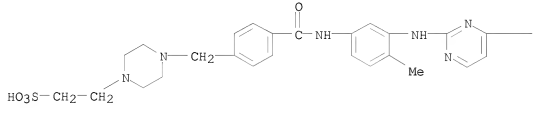
PAGE 2-A

RN 726192-56-9 CAPLUS
CN Benzamide, 4-[(1,1-dioxido-3-oxo-1,2,5-thiadiazolidin-2-yl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



RN 726192-57-0 CAPLUS
CN 1-Piperazineethanesulfonic acid, 4-[[4-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]phenyl]methyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

L22 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:20664 CAPLUS
DN 140:77165
TI Preparation of 4-[(4-methylpiperazin-1-yl)methyl]benzamide for treatment of leukemia
IN Asaki, Tetsuo; Hamamoto, Taisuke; Sugiyama, Yukiteru
PA Nippon Shinyaku Co., Ltd., Japan
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

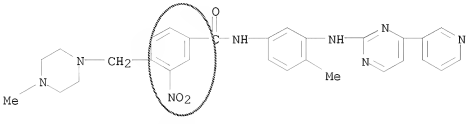
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002963	A1	20040108	WO 2003-JP8192	20030627
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2490907	A1	20040108	CA 2003-2490907	20030627
	AU 2003246100	A1	20040119	AU 2003-246100	20030627
	BR 2003012288	A	20050412	BR 2003-12288	20030627
	EP 1533304	A1	20050525	EP 2003-738555	20030627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1678590	A	20051005	CN 2003-820146	20030627
	MX 2004PA12845	A	20050224	MX 2004-PA12845	20041216
	US 2006014742	A1	20060119	US 2004-519722	20041228
PRAI	JP 2002-189269	A	20020628		
	JP 2002-305146	A	20021018		
	JP 2002-377937	A	20021226		
	WO 2003-JP8192	W	20030627		

OS MARPAT 140:77165
AB The title compds. I [wherein R1 = saturate cyclic amino, alkylamino, or dialkylamino; R2 = alkyl, halo, haloalkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, acyl, amino, alkylamino, dialkylamino, NO2, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, or CN; R3 = H, halo, or alkoxy; Het1 = pyridyl, Ph, pyrimidyl, pyrazinyl, or triazinyl; Het2 = pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, or 1,2-dihydropyridazinyl; etc.] or salts thereof are prepared as BCR-ABL tyrosine kinase inhibitors, and are useful for the treatment of leukemia (no data). For example, the compound II was prepared in a multi-step synthesis. II showed inhibitory activities with IC50 of 0.0008 and 3.99 μM against cell proliferation of K562 and U937, resp., in cow. Formulations containing I as an active ingredient were also described.
IT 641615-04-5P 641615-05-6P 641615-07-8P
641615-08-9P 641615-15-8P 641615-21-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of [(piperazinyl)methyl]benzamides for

treatment of leukemia)

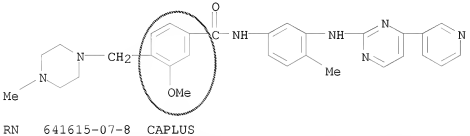
RN 641615-04-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-3-nitro- (CA INDEX NAME)



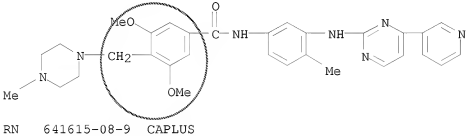
RN 641615-05-6 CAPLUS

CN Benzamide, 3-methoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



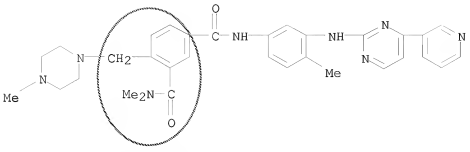
RN 641615-07-8 CAPLUS

CN Benzamide, 3,5-dimethoxy-4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

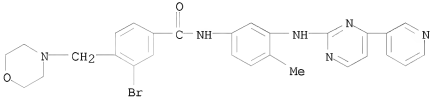


RN 641615-08-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N3,N3-dimethyl-4-[(4-methyl-1-piperazinyl)methyl]-N1-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)

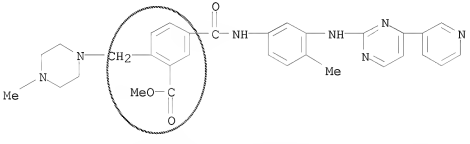


RN 641615-15-8 CAPLUS
CN Benzamide, 3-bromo-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



no N-oxide or oxo substituent on A

RN 641615-21-6 CAPLUS
CN Benzoic acid, 2-[(4-methyl-1-piperazinyl)methyl]-5-[[[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)

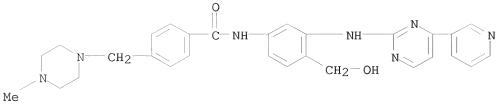


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:591164 CAPLUS
DN 139:149642
TI Preparation of benzoylaminophenylaminopyrimidinylpyridines as antitumor agents
IN Boernsen, Klaus Olaf; End, Peter; Gross, Gerhard; Pfaar, Ulrike
PA Novartis Ag, Switz.; Novartis Pharma Gmbh
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

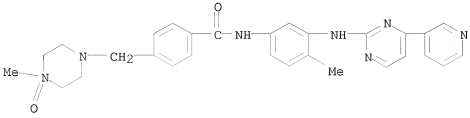
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003062220	A1	20030731	WO 2003-EP613	20030122
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
	CA 2474104	A1	20030731	CA 2003-2474104	20030122
	EP 1470120	A1	20041027	EP 2003-731700	20030122
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003007058	A	20041228	BR 2003-7058	20030122
	JP 2005519908	T	20050707	JP 2003-562099	20030122
	CN 1646519	A	20050727	CN 2003-802708	20030122
	EP 1783126	A2	20070509	EP 2007-101787	20030122
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, SE, SI, SK, TR, RO				
	IN 2004CN01599	A	20060224	IN 2004-CN1599	20040720
	MX 2004PA07130	A	20041029	MX 2004-PA7130	20040723
	US 2005209452	A1	20050922	US 2005-502291	20050429
PRAI	GB 2002-1508	A	20020123		
	EP 2003-731700	A3	20030122		
	WO 2003-EP613	W	20030122		

OS MARPAT 139:149642
AB Title compds. I [R1 = , OH; R2 = H, alkyl, hydroxyalkyl; A = NR3R4, CR3R4, OR3R4; R3R4 = (un)substituted alkylene, oxaalkylene, azaalkylene; at least one N atom is substituted by O] were prepared for use as antitumor agents (no data). Thus, I [R1 = H, R2 = Me, A = 4-methyl-4-oxido-1-piperazinyl] was prepared by oxidation of I [R1 = H, R2 = Me, A = 4-methyl-1-piperazinyl].
IT 571186-90-8P 571186-91-9P 571186-92-0P
571186-93-1P 571186-94-2P 571186-95-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzoylaminophenylaminopyrimidinylpyridines as antitumor agents)
RN 571186-90-8 CAPLUS
CN Benzamide, N-[4-(hydroxymethyl)-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



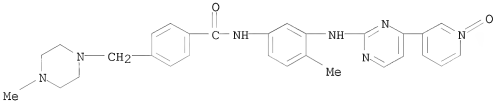
claim 33

RN 571186-91-9 CAPLUS
CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



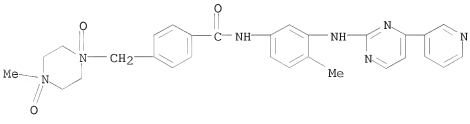
claim 30

RN 571186-92-0 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(1-oxido-3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)



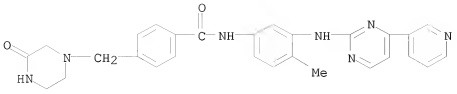
claim 31

RN 571186-93-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1,4-dioxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



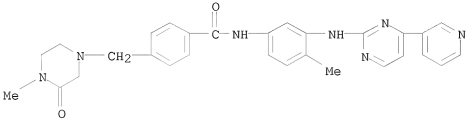
claim 32

RN 571186-94-2 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(3-oxo-1-piperazinyl)methyl]- (CA INDEX NAME)



Claim 25

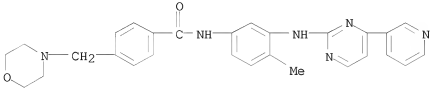
RN 571186-95-3 CAPLUS
CN Benzamide, 4-[(4-methyl-3-oxo-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



claim 26

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:409452 CAPLUS
DN 139:226295
TI Two distinct phosphorylation pathways have additive effects on Abl family kinase activation
AU Tanis, Keith Q.; Veach, Darren; Duewel, Henry S.; Bornmann, William G.; Koleske, Anthony J.
CS Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT, 06520, USA
SO Molecular and Cellular Biology (2003), 23(11), 3884-3896
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB The activities of the related Abl and Arg nonreceptor tyrosine kinases are kept under tight control in cells, but exposure to several different stimuli results in a two- to fivefold stimulation of kinase activity. Following the breakdown of inhibitory intramol. interactions, Abl activation requires phosphorylation on several tyrosine residues, including a tyrosine in its activation loop. These activating phosphorylations have been proposed to occur either through autophosphorylation by Abl in trans or through phosphorylation of Abl by the Src nonreceptor tyrosine kinase. The authors show here that these two pathways mediate phosphorylation at distinct sites in Abl and Arg and have additive effects on Abl and Arg kinase activation. Abl and Arg autophosphorylate at several sites outside the activation loop, leading to 5.2- and 6.2-fold increases in kinase activity, resp. The authors also find that the Src family kinase Hck phosphorylates the Abl and Arg activation loops, leading to an addnl. twofold stimulation of kinase activity. The autoactivation pathway may allow Abl family kinases to integrate or amplify cues relayed by Src family kinases from cell surface receptors.
IT 404843-98-7, WGB-BC 22
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(inhibitor; drug sensitivities of Abl and Arg kinases)
RN 404843-98-7 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



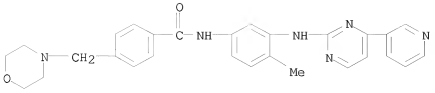
no N-oxide or oxo substituent on A

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:220573 CAPLUS
DN 136:247605
TI N-phenyl-2-pyrimidinamine derivatives as tyrosine kinase inhibitors
IN Buerger, Hans Michael; Caravatti, Giorgio; Zimmermann, Juerg; Manley, Paul William; Breitenstein, Werner; Cudd, Margaret Amelia
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022597	A1	20020321	WO 2001-EP10503	20010911
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2416274	A1	20020321	CA 2001-2416274	20010911
	AU 200218167	A	20020326	AU 2002-18167	20010911
	BR 2001013838	A	20030603	BR 2001-13838	20010911
	EP 1322634	A1	20030702	EP 2001-984640	20010911
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004509111	T	20040325	JP 2002-526850	20010911
	CN 1525967	A	20040901	CN 2001-815539	20010911
	CN 1872850	A	20061206	CN 2006-10100258	20010911
	US 2004102453	A1	20040527	US 2003-363841	20030310
	US 7081532	B2	20060725		
	US 2006223818	A1	20061005	US 2006-448649	20060607
PRAI	GB 2000-22438	A	20000913		
	CN 2001-815539	A3	20010911		
	WO 2001-EP10503	W	20010911		
	US 2003-363841	A3	20030310		

OS MARPAT 136:247605
AB The N-phenyl-2-pyrimidinamines I [R = substituted Ph; R1 = (un)substituted pyrazinyl, 1-methylpyrrolyl, aminophenyl, aminoalkylphenyl, indolyl, imidazolyl, pyridyl, pyridyl N-oxide; R2, R3 = H, alkyl] were prepared for use as tyrosine kinase inhibitors with IC50 of 3-300 nM. Thus, the benzamide II [R4 = 4-ethylpiperazino] was prepared from II [R4 = Cl] and 1-ethylpiperazine.
IT 404843-98-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-phenyl-2-pyrimidinamine derivs. as tyrosine kinase inhibitors)
RN 404843-98-7 CAPLUS
CN Benzamide, N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-(4-morpholinylmethyl)- (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              74.25     434.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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